MEMORANDUM:

Subject: EPA File Symbol/EPA Reg. No.:279-GRGN

From: Lucy D. Markarian, Biologist 3/12/92
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

To: George LaRocca, PM 13
Insecticide-Rodenticide Branch
Registration Division (H7505C)

Thru: Thomas C. Ellwanger, Section Head E 3/10/92
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

Applicant: FMC Corporation
Agricultural Chemical Group
1735 Market Street
Philadelphia, PA 19103

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Bifenthrin: (2-methyl[1,1'-biphenyl]-3-yl) methyl-3-(2-chloro-3,3,3-trifluoro-1-propenyl) -2,2-dimethylcyclopropane-carboxylate	0.2 %
Inert Ingredient(s):	99.8 %
Total:	100.0 %

BACKGROUND

FMC corporation has applied for the registration of Talstar Granular insecticide/ miticide containing bifenthrin as active ingredient. This is to be used against imported fire ants. Currently the USDA is working towards the certification of bifentrin as part of its Imported Fire Ant-Free Nursery Program. Six acute tests are submitted to support the registration as well as a request for the waiver of the inhalation study that is based on the following premises:

1-The base of this product is [redacted], meaning that the smallest particle size would be approximately 400 microns, and the tests conducted for manufacturing purposes at FMC have found the smallest particle to be 50 microns.

2-The vapor Pressure of bifenthrin is 1.81×10^{-7} mm hg at 25° $_{o}$C indicating the non volatile state of the formulation.

3-The use pattern of the product would make inhalation a negligible routeof exposure. The insecticide is applied to a bulk amount of soil and mechanically incorporated into the soil. The ratio of bifenthrin to soil would be 50 ppm.

RECOMMENDATION

The submitted tests are acceptable support for the registration. The rationale for the ratings is given below.

The waiver request cannot be granted on the basis of the given reasons. All testing is done under exaggerated conditions to define the toxicity potential. While the [redacted] base of the formulation is considered, PRS is more concerned about the generation of the fines while being handled by the users. The product at points must be handled by poeple. The vapor pressure is not of concern when a solid such as this product is in consideration. The inhalation waiver may be considered if FMC could present an actual particle size analysis of the product and can prove that it is not possible to grind it fine enough to generate an aerosol to be tested. This is requested of all applicants.

Oral toxicity- core minimum

The use of margarine as the medium was unusual. There was no assurance that the test material was evenly distributed in the medium. The usual medium is corn oil which allows the maintenance of homogeneity by visual observation and constant stirring during the intubation.

Dermal toxicity in rats- and rabbits-Dermal irritation in rabbits- core minimum

The introduction of methanol to the test system is not explained. The use of methanol does not seem necessary considering the nature of the test material.

Dermal sensitization- Core minimum

1-Introduction of methanol into the test system adds an unnecessary variable and is not explained.

2-It is required by the guidelines that the selected test method be stated. The methodology used appears to be the Buehler method; therefore it was evaluated as one. the inclusion of the name of the method is encouraged.

3- While it is not necessary that every test include a positive control in a sensitization test, reference must be given to a positive control study performed at the laboratory within three months of the date of the presented study to show the capability of the laboratory to induce sensitization. No positive controls were included in the presented test, nor any reference was given to a positive control study performed in the laboratory as described above.

4- PRS encourages all laboratories to grade the test by the method devised by the author of the method. Grading a Buehler test by the Draize system is not always accurate due to the different approaches of each respective author. The Draize system is graded in approach and is primarily for primary dermal evaluations. The Buehler approach is more quantal in approach, and gradations come into play only if there is irritation in the naive control group, or if it is necessary to evaluate the severity of the immune response. In all other cases irritation is either present or is not regardless of degree of erythema and edema observed.

LABELING

The signal word is CAUTION as it appears on the proposed label. The precautionary label is adequate at this time. If an inhalation test is deemed necessary, after the required data is presented, the label may have to be revised.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1)

Product Manager: 13 **Reviewer:** L. Markarian
MRID No.: 420942-02 **Report Date:** 3/19/92
Testing Facility: FMC Corp. Toxicology Lab. **Report No.** A90-3157
Author(s): Christine Freeman
Species: Rat, Sprague Dawley
Age: Young adult
Weight: Males 231 - 289, Females 217 - 233 g
Source: Taconic Farms, Germantown, NY
Test Material: Bifenthrin 0.2 % granules, reference No PL89-160
Quality Assurance (40 CFR §160.12): Included

Conclusion:

1. The estimated LD_{50} is > 5000 mg/kg
2. Tox. Category: IV Classification: core minimum

Procedure (Deviations from §81-1):

The test material was administered to fasted rats as a 25 %w/v mixture in margarine by intubation with a plastic catheter. Observations were at 1/2, 1/ 2, 3, 4, and 6 hours after administration and daily thereafter. Body weights were recorded at initiation and on days 7 and 14. Necropsy was performed on all animals.

Results:

Dosage mg/kg	(Number Killed/Number Tested)		
	Males	Females	Combined
5000	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings:

Symptoms of toxicity included perineal staining and diarrhea. All animals were normal on day 3. Necropsy revealed no abnormalities.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager:13 **Reviewer:** L. Markarian
MRID No.: 420942-03 **Report Date:**3/18/92
Testing Laboratory:FMC Corp. Toxicology Lab. **Report No.:**A90-3162
Author(s): Christine Freeman
Species: Rat, Sprague Dawley
Weight: Males 282 - 300 g, Females 272 - 287 g
Source: Taconic Farms, Germentown, NY
Test Material: Bifenthrin 0.2 % granules Reference No PL89-160
Quality Assurance (40 CFR §160.12): Included

Summary:

1. **The estimated LD_{50} is** > 2000 mg/kg

2. **Tox. Category:** III **Classification:**core minimum

Procedure (Deviation From §81-2):

The test material was weighed on 2 x 2 inch 8 ply gauze pad, moistened with saline, and applied to the shaved skin of the rats. It is not stated where on the animal this was applied. The pads were held in place with tape and the trunks of the animals were wrapped in elastic bandage. At 24 hrs the wrappings were removed and the sites wiped with clean gauze moistened with methanol and rinsed with tap water. No reason is given for the use of methanol. Observations were at 1/2, 1, 2, 3, 4, and 6 hours after application and twice daily thereafter. Body weights were recorded at initiation and on days 8 and 14. Necropsy was performed on all animals.

Results:

Reported Mortality

DOSAGE mg/kg	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings:

There were no deaths. Sins of toxicity included chromorhinorrhea and diarrhea observed up to six hours after administration. All animals remained normal during the remainder of the observation period. Necropsy revealed no gross pathology.

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: 13 **Reviewer:** L. Markarian
MRID No.: 420942-04 **Report Date:** 3/18/92
Testing Laboratory: FMC Corp. Toxicology Lab. **Report No.:** A90-3158
Author(s): Christine Freeman
Species: Rabbit, New Zealand white
Weight: 2.18 - 2.69 K
Source: Hazleton Research Animals, Inc., Denver, PA
Test Material: Bifenthrin 0.2 % granular, Reference No PL89-160
Quality Assurance (40 CFR §160.12): Included

Summary:

1. The estimated LD_{50} is > 2000 mg/kg

2. Tox. Category: III **Classification:** core minimum

Procedure (Deviation From §81-2):

The test material was weighed onto an 4 x 4 inch 8 ply gauze pad, moistened with saline and applied to the shaved skin. The pad was secured with tape and the trunks of the animals were wrapped with plastic sheeting. At 24 hours the wrappings were removed and the sites were wiped with methanol and rinsed with tap water. Observations were at 1/2, 1, 2, 3, and 4 hrs after application and twice daily thereafter. Body weights were recorded at initiation and on days 7 and 14 and at death. Necropsy was performed on all rabbits.

Results:

Reported Mortality

DOSAGE mg/kg	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2000	0/5	1/5	1/10

Symptoms & Gross Necropsy Findings:

One animal died of a broken back shortly after application. No systemic toxicity was observed. Dermal irritation was expressed as erythema and desquamation in one animal each. Necropsy revealed no abnormalities.

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 13 **Reviewer:** L. Markarian
MRID No.: 420942-05 **Report Date:** 3/18/92
Testing Laboratory: FMC Corp. Toxicology Lab. **Report No.:** A90-3159
Author(s): Christine Freeman
Species: Rabbit, New Zealand White
Sex: 3 male and 3 female
Weight: 2.37 - 3.63 K
Source: Hazleton Research animals, Inc., Denver, PA
Dosage: 0.1 g
Test Material: Bifenthrin 0.2 % granules, Reference No PL89-160
Quality Assurance (40 CFR §160.12): Included

Summary:

1. **Toxicity Category:** IV

2. **Classification:** Guideline

Procedure (Deviations From §81-4):

Test material as received was instilled in the conjunctival sacs of pre examined eyes. Observations were at 1, 24, 48, and 72 hrs. corneal findings were confirmed with fluorescein. Scoring was according to Draize.

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	0/6	0/6	0/6				
Iris	0/6	0/6	0/6	0/6				
Conjunctivae								
Redness	0/6	0/6	0/6	0/6				
Chemosis	0/6	0/6	0/6	0/6				
Discharge	0/6	0/6	0/6	0/6				

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: 13 **Reviewer:** L. Markarian
MRID No.: 420942-06 **Report Date:** 2/18/92
Testing Laboratory: FMC Corp. Toxicology Lab. **Report No.:** A90-3160
Author(s): Christine Freeman
Species: Rabbit, New Zealand White
Age: Young adult
Sex: Three male and three female
Weight: 2.35 - 2.85
Dosage: 0.5 g
Test Material: Bifenthrin 0.2 % granular, Reference No PL89-160
Quality Assurance (40 CFR §160.12): Included

Summary:

1. The Primary Irritation Index =0
2. Toxicity Category: IV
3. Classification: ~~Guideline~~ MINIMUM E

Procedure (Deviations From §81-5):

The test material was weighed on 2 x 2 inch 8 ply gauze pas, moistened and applied to the shaved skin of rabbits. The patches were secured with tape and the trunks were wrapped in gauze bandage. The wrappings were removed at 4 hrs and the sites were wiped with methanol and rinsed with tap water.
The sites were evaluated at 1, 24, 48, and 72 hrs according to Draize.

Results:

No irritation was observed at any site on any of the animals at any interval.

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager:13 **Reviewer:** L. Markarian
MRID No.: 420942-07 **Report Date:**3/18/92
Testing Laboratory:FMC Corp. Toxicology Lab. **Report No.:** A90-3161
Author(s): Christine Freeman
Species: Guinea Pig, Hartley
Weight: 304 to 359 g
Source: Hazleton Research Animals, Inc.,Denver, PA
Test Material: Bifenthrin 0.2 % granules, Reference No PL89-160
Positive Control Material:NONE
Quality Assurance (40 CFR §160.12): Included

Method: Assumed to be Buehler method , not stated

Summary:

1. **This Product is not a dermal sensitizer.**

2. **Classification:** Core minimum

Procedure (Deviation From §81-6):

A pre test irritation screening was made using 100% test material and two guinea pigs. No irritation was observed .Induction and elicitation were conducted at 100 %. 0.3 mg aliquots were used in hill top chambers for the three induction and challenge applications. Inductions were once a week for three weeks for six hours. The applications were made in Hilltop chambers and the test material was moistened. The same site was used for all inductions, but a naive site was used for the challenge. The chambers were held in place with tape. No restrainers were used. At the removal of the applications the sites were wiped with methanol and rinsed with tap water. Twenty animals, ten male and ten female were used in the test group. Five male and five female animals were used as naive controls and received challenge applications only.
The sites were evaluated at 24 and 48 hours after applications according to Draize.
There were no positive controls and no reference was made to any positive control results that the laboratory may have had.

Results:

No irritation was observed at any site on any animal at any interval. All naive controls were negative.

Chem Tox No. could not be found Current Date 3/18/92

Laboratory: FMC Corporation, Toxicology Laboratory
Box 8, Princeton NJ 08543

STUDY	MATERIAL	MRID NO	RESULTS	TOX CAT	CORE GRADE
Oral Toxicity Limit test (rats) A90-3157 3/29/90	Bifenthrin 2 % granules Reference # PL89-160	420942-02	LD_{50} >5000 mg/kg	IV	minimum
Dermal Toxicity Limit Test (rats) A90-3162 3/20/90	" " "	420942-03	LD_{50} >2000 mg/kg	III	minimum
Dermal Toxicity Limit Test(rabbits) A90-3158 3/30/90	" " "	420942-04	LD_{50} > 2000 mg/kg	III	minimum
Eye Irritation in Rabbits A90-3159 3/5/90	" " "	420942-05	None irritating	IV	guideline
Dermal Irritation in Rabbits A90-3160 3/13/90	" " "	420942-06	Nonirritating	IV	minimum
Dermal Sensitization In Guinea Pigs A90-3161 3/29/90	" "	420942-07	Non sensitizer	NA	minimum